Targeting oncogenic microRNAs in Triple Negative Breast Cancer using CRISPR/cas9 approach

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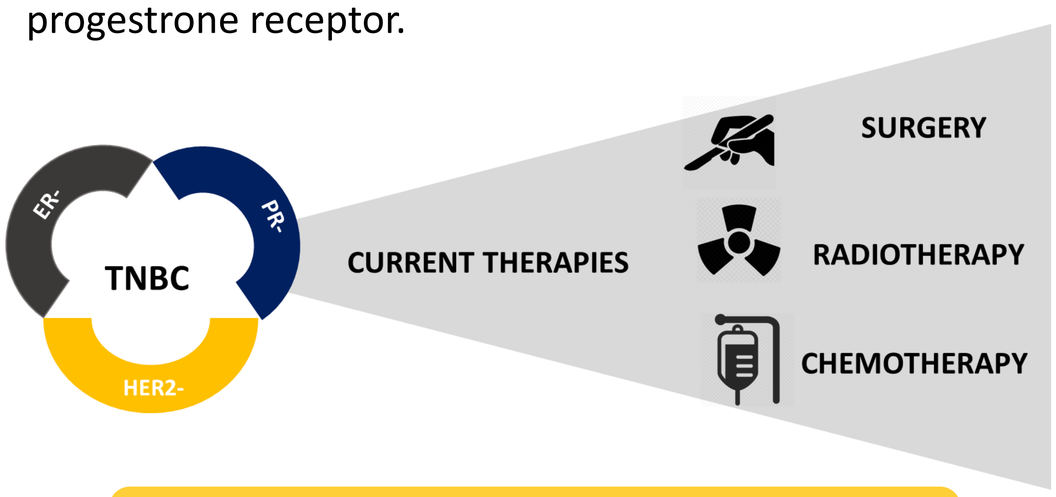
Introduction

Triple negative breast cancer (TNBC) represents **15-20% of breast cancer cases** (about 2 out of every 10 cases).

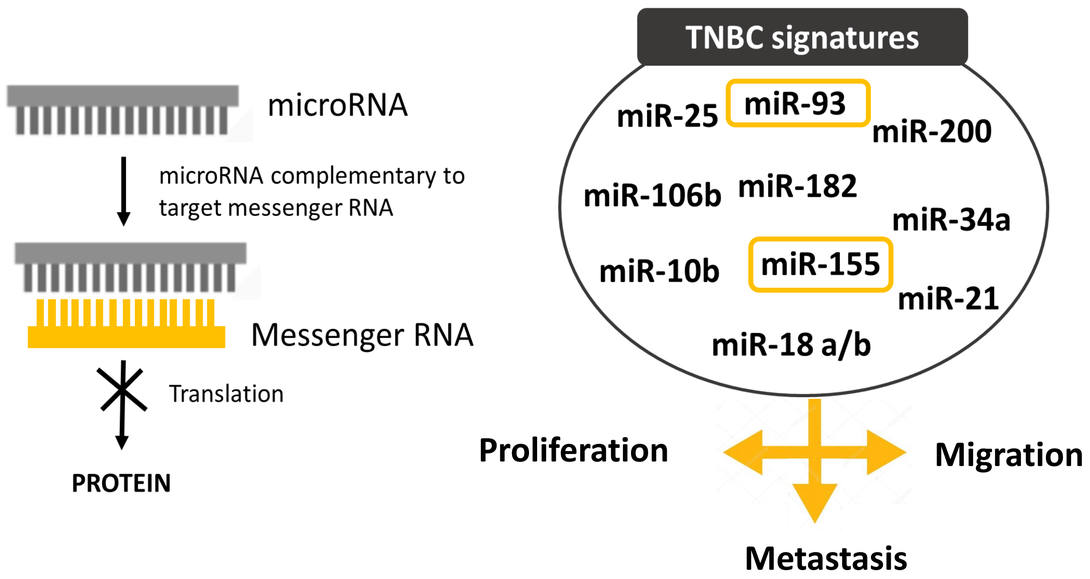
Characterized by the absence of three biomarkers: human epidermal growth factor receptor 2, estrogen and progestrone receptor.



Treatment is a major clinical challenge due to **lack of targeted therapy**

Methodologies

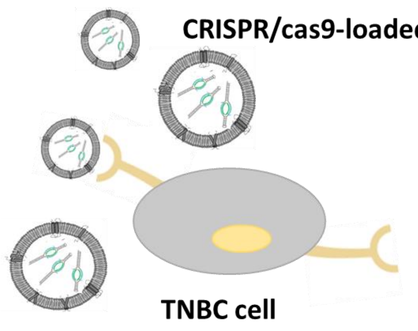
Dysregulation of microRNAs was involved in the initiation of oncogenesis. Many **microRNAs have been associated to TNBC due to their overexpression** in this cancer subtype.



CRISPR/cas9 is a powerful genome-editing tool able to **knockout the expression of oncogenic microRNAs**

Exosomes as a delivery platform of CRISPR/cas9 system in TNBC

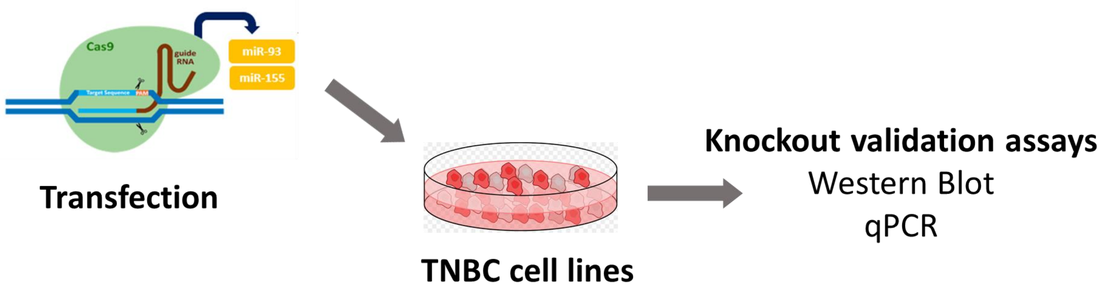
Main Goal



Efficient TNBC therapy comprising of exosomes loaded with CRISPR/cas9 system against oncogenic microRNAs

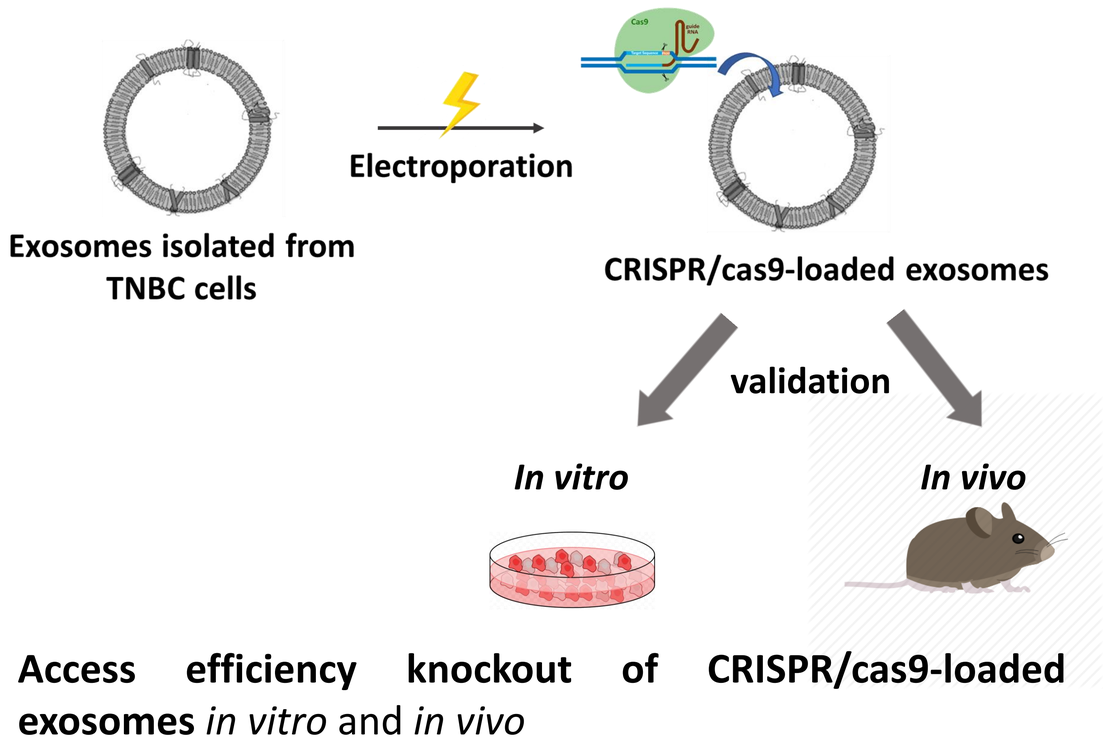
Objectives

Construction of CRISPR/cas9 system against microRNAs upregulated in TNBC cases.



Transfection of CRISPR/cas9 system to **knockout oncogenic microRNAs in TNBC cells.**

Incorporation of CRISPR/cas9 system in exosomes to improve intracellular delivery.



Access efficiency knockout of CRISPR/cas9-loaded exosomes *in vitro* and *in vivo*

References

[1] X. Dai, L. Xiang, T. Li, and Z. Bai, "Cancer Hallmarks, Biomarkers and Breast Cancer Molecular Subtypes," *J. Cancer*, vol. 7, no. 710, pp. 1281–1294, 2016.
[2] X. Mao, P. Shi, B. He, K. Xu, S. Zhang, and J. Wang, "MicroRNAs in the prognosis of triple-negative breast cancer," vol. 0, no. January, 2017.
[3] J. Zhang, S. Li, L. Li, M. Li, C. Guo, J. Yao, and S. Mi, "Exosome and Exosomal MicroRNA: Trafficking, Sorting, and Function," *Genomics. Proteomics Bioinformatics*, vol. 13, no. 1, pp. 17–24, Feb. 2015.